

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A process for the production of a biologically active protein selected from the group consisting of G-CSF, GM-CSF, M-CSF, EGF, HAS, DNase, FGF, TNF-alpha, TNF-beta, interferons, and interleukins, comprising:

expressing said protein as a heterologous protein in an expression system comprising a cultivated organism having at least one cell ~~or more cells~~, wherein the protein is expressed as a substantially correctly folded protein precursor, wherein the protein precursor has an aqueous solubility, in non-classical inclusion bodies ~~having an aqueous solubility in the cells of the organism;~~

regulating one or more cultivation parameters selected from the group consisting of temperature of cultivation, composition of cultivation medium, induction mode, principle of performing the fermentation, addition of a stress induction agent ~~an agent capable of causing stress,~~ and co-expression of auxiliary proteins, wherein regulating the one or more parameters increases the proportion of substantially correctly folded protein precursor present in the non-classical inclusion bodies in the cell[[s]], relative to the proportion of substantially correctly folded protein precursor present in inclusion bodies in a cell[[s]] of an organism not cultivated by regulating said parameters;

isolating the non-classical inclusion bodies from the cell[[s]] of the organism;

optionally, washing the non-classical inclusion bodies;

solubilizing the substantially correctly folded protein precursor from the non-classical inclusion bodies under non-denaturing conditions by contacting the non-classical inclusion bodies with a non-denaturing aqueous solvent having a pH of about 8.0; and

purifying the biologically active protein from the solubilized substantially correctly folded protein precursor and non-denaturing aqueous solvent,

wherein the process for the production of the biologically active protein is free from any denaturation and renaturation of the protein.

2. (Canceled).
3. (Cancelled).
4. (Previously Presented) A process for the production of a protein according to claim 1, wherein the selected heterologous protein is G-CSF.
5. (Previously Presented) A process for the production of a protein according to claim 1, wherein the cultivated organism is selected from the group consisting of bacteria and yeasts.
6. (Previously Presented) A process for the production of a protein according to claim 5, wherein the cultivated organism is the bacterium *E. coli*.
7. (Previously Presented) A process for the production of a protein according to claim 1, wherein the heterologous protein is accumulated in the inclusion bodies to a proportion of at least about 10%, relative to the total protein mass of a cell of the organism used in the expression system.
8. (Canceled).
9. (Canceled).
10. (Previously Presented) A process according to claim 1, wherein the temperature of cultivation ranges from about 20° C to about 30° C.
11. (Canceled).
12. (Previously Presented) A process according to claim 1, wherein regulating the induction mode comprises selecting an inducer from the group consisting of IPTG, lactose, and NaCl.
13. (Previously Presented) A process according to claim 12, wherein the selected inducer is IPTG.

14. (Previously Presented) A process according to claim 13, wherein the concentration of IPTG ranges from about 0.1 mM to about 1 mM.
15. (Previously Presented) A process according to claim 14, wherein the concentration of IPTG is about 0.4 mM.
16. (Previously Presented) A process according to claim 12, wherein the regulation of the induction mode further comprises adding the inducer at the beginning of the fermentation.
17. (Previously Presented) A process according to claim 1, wherein the principle of performing the fermentation is selected from the group consisting of performing of fermentation in a batch mode, performing of fermentation in a fed batch mode and performing of fermentation in one or more shake flasks.
18. (Canceled).
19. (Previously Presented) A process according to claim 1, wherein the composition of the cultivation medium is selected from the group consisting of GYST, GYSP, LYSP, LYST, LBON and GYSPON.
20. (Previously Presented) A process according to claim 19, wherein the selected medium is GYST; or GYSP.
21. (Currently Amended) A process according to claim 1, wherein the stress induction agent ~~agent~~ ~~additive which is capable of causing stress~~ is selected from the group consisting of ethanol and propanol.
22. (Canceled).

23. (Previously Presented) A process according to claim 1, wherein the step of washing comprises contacting the inclusion bodies with a solution selected from the group consisting of Tris/HCl buffer, phosphate buffer, acetate buffer, citrate buffer and water.
24. (Previously Presented) A process according to claim 23, wherein the concentration of the selected buffer ranges from about 1 mM to about 10 mM.
25. (Previously Presented) A process according to claim 23, wherein the selected solution is water.
26. (Currently Amended) A process for production of a protein according to claim 1, wherein the ~~step of solubilizing the substantially correctly folded protein precursor from the inclusion bodies further comprises contacting the inclusion bodies with~~ non-denaturing aqueous solvent solution is selected from the group consisting of aqueous solutions of: urea ranging in concentration from about 1M to about 2M, N-lauroyl sarcosine ranging in concentration from about 0.05% to about 0.25% mass per volume, betain, sarcosine, carbamoyl sarcosine, taurine, DMSO, non-detergent sulfobetains, and a buffer in a high, solubilising concentration, said buffer being selected from the group consisting of HEPES, HEPPS, MES, and ACES.
- 27-37. (Canceled).
38. (Currently Amended) The process of claim 26, wherein the non-denaturing aqueous solvent solution is comprises a relatively low concentration of N-lauroyl sarcosine in water, in order to avoid denaturing conditions.
39. (Previously Presented) The process of claim 38, wherein the concentration of N-lauroyl sarcosine further ranges from about 0.1% to about 0.25% mass per volume.
40. (New) The process of claim 4, wherein the specific activity of the G-CSF is at least 1×10^7 IU/mg.

41. (New) The process of claim 1, wherein the amount of protein expressed is at least about 20% by mass of the total mass of proteins produced by the host cell.
42. (New) The process of claim 1, wherein the amount of protein expressed is at least about 30% by mass of the total mass of proteins produced by the host cell.